Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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P-POSSUM as mortality predictor in COVID-19-infected patients submitted to emergency digestive surgery. A retrospective cohort study

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ABSTRACT

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Background: COVID-19 infection is associated with a higher mortality rate in surgical patients, but surgical risk scores have not been validated in the emergency setting. We aimed to study the capacity for postoperative mortality prediction of the P-POSSUM score in COVID-19-positive patients submitted to emergency general and digestive surgery.

Material and methods: Consecutive patients undergoing emergency general and digestive surgery from March to June 2020, and from March to June 2019 in 25 Spanish hospitals were included in a retrospective cohort study. Main outcome: 30-day mortality. P-POSSUM discrimination was quantified by the area under the curve (AUC) of ROC curves; calibration was assessed by linear regression slope (β estimator); and sensitivity and specificity were expressed as percentage and 95% confidence interval (CI).

Results: 4988 patients were included: 177 COVID-19-positive; 2011 intra-pandemic COVID-19-negative; and 2800 pre-pandemic. COVID-19-positive patients were older, with higher surgical risk, more advanced pathologies, and higher P-POSSUM values (1.79% vs. 1.09%, $p < 0.001$, in both the COVID-19-negative and control cohort). 30-day mortality in the COVID-19-positive, intra-pandemic COVID-19-negative and pre-pandemic cohorts were: 12.9%, 4.6%, and 3.2%. The P-POSSUM predictive values in the three cohorts were, respectively: AUC 0.88 (95% CI 0.81–0.95), 0.89 (95% CI 0.87–0.92), and 0.91 (95% CI 0.88–0.93); β value 0.97 (95% CI 0.74–1.2), 0.99 (95% CI 0.82–1.16), and 0.78 (95% CI 0.74–0.82); sensitivity 83% (95% CI 61–95), 91% (95% CI 84–96), and 89% (95% CI 80–94); and specificity 81% (95% CI 74–87), 76% (95% CI 74–78), and 80% (95% CI 79–82).

Conclusion: The P-POSSUM score showed a good predictive capacity for postoperative mortality in COVID-19-positive patients submitted to emergency general and digestive surgery.

1. Introduction

Patients submitted to emergency surgeries are at higher risk of postoperative complications and mortality, compared to those undergoing elective interventions [1,2]. Early identification of high-risk patients by adequate surgical prognostic estimation is crucial for clinical decision-making, prompt escalation of care, and health resource management [1–5]. Among the several risk predictive tools that have been designed and tested in the emergency surgery setting, the Physiological and Operative Severity Score for the enUmeration of Mortality and Morbidity (POSSUM) is maybe the most widely validated and used in clinical practice [6]. It is based on clinical and analytical data obtained before and during the surgical intervention regarding the patients' comorbidities, their physiological condition, the severity of their surgical pathology and the type of the surgical intervention. With the aim of improving the predictive capacity of the original POSSUM score, a modified score was designed in 1996, called Portsmouth-POSSUM (P-POSSUM), and since then it has been widely used for surgical patients worldwide [7,8].

Coronavirus disease (COVID-19), caused by SARS-CoV-2 virus, has spread globally since December 2019, causing more than 4.4 million deaths (to date August 27th, 2021) and stressing health-care systems worldwide [9–11]. COVID-19-infected patients submitted to elective or emergency surgical interventions appear to be susceptible to poorer postoperative outcomes, probably due to synergistic immunological dysregulation, hyperinflammatory response to surgery, and need of mechanical ventilation [12–16]. However, a general recommendation of delaying all surgical interventions in COVID-19-positive patients is not applicable, as not all emergency interventions can be avoided without considerable life risk for the patient. Therefore, an estimation of the postoperative risk in these patients is needed, in order to be balanced against the risk of delaying surgery in each individual case. Available prognostic tools for non-surgical COVID-19-infected patients are of limited help in the surgical setting [17,18], and usual surgical risk calculators such as P-POSSUM have not been tested in COVID-positive patients.

The aim of this study was to estimate the predictive capacity of the P-POSSUM score for postoperative 30-day mortality in COVID-19-positive patients submitted to emergency general and digestive surgery, compared to COVID-19-negative and pre-pandemic patients.

2. Material and methods

2.1. Study design and participants

This is a retrospective cohort study including all consecutive adult patients operated on for urgent digestive pathology between March 1st and June 30th, 2020, and during the same period of the previous year, in 25 Spanish hospitals. Patients with missing data needed for the calculation of the P-POSSUM score and/or without ≥30 days postoperative follow-up were excluded.

Three cohorts were prospectively defined:

a) Cohort 1: COVID-19-positive patients operated between March 1st and June 30th, 2020;
b) Cohort 2: COVID-19-negative patients operated during the same period time;
c) Cohort 3: patients operated between March 1st and June 30th, 2019 (pre-pandemic cohort).

Pre- and intra-pandemic COVID-19-negative patients were analysed separately because raw 30-day mortality of both groups might differ, as previously described, probably due to the different context in which clinical care was provided [19].

COVID-19 infection was assessed by reverse-transcriptase-polymerase-chain-reaction test (RT-PCR) on nasopharyngeal swab.

The study protocol was approved by the Clinical Research Ethics Committee of the leading and collaborating centers, and it has been previously published [20]. Patients' informed consent was waived given the retrospective nature of the study. The study was designed in compliance with the principles of the Declaration of Helsinki and reported following the recommendations of the STROCSS 2019 guideline [21]. Confidentiality was guaranteed in accordance with current Spanish legislation (LOPD 3/2018). Official study registry: ClinicalTrials.gov NCT04479150, July 21st, 2020. The COVID-CIR project has been awarded a research grant, intended entirely for electronic Case Report Form design and statistical analysis.

2.2. Data collection, variables, and outcomes

This study was based in the multicenter COVID-CIR registry, including data from electronic medical records by the participating hospitals (COVID-CIR Collaborative Group, fully detailed in Supplemental file) [20]. Anonymized data were entered into an electronic Case Report Form (eCRF), based on the REDCap® platform (Research

Electronic Data Capture) [22]. Before analysis, the principal investigators (JO, ZM and SV) confirmed completeness and accuracy of data with senior surgeons from each center. Demographic data included: age, sex, body mass index, ASA (American Society of Anesthesiologists) score [23], functional status [24], arterial hypertension, diabetes, smoking, chronic obstructive pulmonary disease (COPD) and cardiovascular disease.

The P-POSSUM risk scoring system is based on 12 preoperative parameters [6–8]: age, cardiac system, respiratory system, systolic blood pressure, heart rate, Glasgow coma score, electrocardiographic findings, and urea, sodium, potassium, hemoglobin and leukocyte values; and on 6 intraoperative variables [6–8]: surgical complexity, number of surgical procedures, blood loss, peritoneal fluid appearance, neoplasm and surgical priority. Complexity of procedures was categorized as "minor, moderate, major or major-plus", according to the original definitions of the POSSUM score [6]. Surgical priority was classified as "emergency", if surgery was required within 2 h from arrival at the emergency department, or "urgency", if surgical intervention was required during the first 24 h [6]. Each variable was weighted according to an exponential scoring system and the P-POSSUM score was calculated in each cohort according to the following equation: $\ln [R/(1-R)] = -9.065 + (0.1692 \times \text{physiological score}) + (0.155 \times \text{operative score})$, where R corresponds to the estimated risk of mortality (first 30 postoperative days) [7,8].

Five additional preoperative inflammatory parameters of clinical interest during the COVID-19 pandemic were recorded: C-reactive protein (CRP) value, lymphocyte count, and inflammatory indices NLR (neutrophil/lymphocyte ratio), PLR (ratio platelets/lymphocytes) and SII (systemic immune-inflammation index, neutrophils x platelets/lymphocytes) [9,25].

Main outcome was 30-day mortality. Secondary outcomes were: overall postoperative complications, severe postoperative complications (≥IIIA score on the Clavien-Dindo classification) [26], need for postoperative ICU (Intensive Care Unit) for ≥24 h, length of stay, hospital readmission and surgical reintervention during the first 30 postoperative days.

2.3. Statistical analysis

Due to the descriptive design of the study, calculation of the sample size was not performed, being defined by the number of patients fulfilling inclusion criteria and complete data operated on during the study periods.

Quantitative variables were described by means and standard deviation or median and interquartile range, and qualitative variables by absolute number and percentage. Incidences of complications, pulmonary complications, severe complications and mortality were expressed by percentage and 95% confidence interval (95% CI).

Discrimination is defined as the ability of the score to assign a higher risk of mortality to patients who eventually die and a lower risk to those who survive, and was quantified using the value of the area under the curve (AUC, including its 95% CI) of the Receiver Operating Characteristic graphs (ROC curves) in each cohort [27]. Figures from AUC 0.7–0.8 give a score an acceptable value; AUC 0.8–0.9 values qualify it as excellent; AUC figures >0.9 allow us to consider a score as outstanding [28].

Calibration refers to the ability of a model to predict the response variable. To assess calibration, the expected and observed incidence of each event in deciles of predicted risk was compared graphically. The estimator of the linear regression slope (β value) between the observed and expected incidents in each decile was reported. A slope close to 1 suggests that there are no differences between the observed incidence and that expected by the model; a slope <1 suggests an underestimation of risk by the model; and a slope >1, an overestimation of risk. The slope estimator is accompanied by a 95% CI to facilitate its interpretation.

In order to estimate an optimal cut-off for P-POSSUM score that best discriminates between patients alive and those who died, we used the Youden index maximization method [29]. Bootstrap method was used to determine the 95% CI. With the cut-off in each cohort, sensitivity, specificity, positive and negative predictive values, and positive and negative likelihood ratios were calculated in each cohort and expressed as a value or percentage and 95% CI [29].

Statistical analysis and graphic representations were developed using R version 3.6.3 computer software (R Core Team [2020]. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/). The Chi-squared test and the Student's *t*-test were used for categorical and continuous variables, respectively. [Reviewer #2, comment #8] The Mann-Whitney *U* test was used for not-normally distributed data. Significance was defined as $p < 0.05$.

3. Results

3.1. Patients' characteristics and P-POSSUM score values

The COVID-CIR registry originally included 5307 patients who underwent urgent digestive or general surgery during the study periods. The population of this study is made up of 4988 patients who presented all variables needed to calculate the P-POSSUM score and complete ≥30 days follow-up. Of these operated patients, during the pandemic period 177 tested positive for COVID-19, 2011 tested negative for COVID-19; and 2800 patients correspond to the pre-pandemic period (Fig. 1).

Demographic characteristics, risk factors, comorbidities, functional status, inflammatory parameters, and P-POSSUM score variables of the three cohorts are detailed in Table 1. COVID-19-positive patients, compared to COVID-19-negative ones, were older, with higher ASA scores, more functionally dependent, with more comorbidities, higher inflammatory markers and indexes, higher lymphopenia rate, greater incidence of peritonitis and malignancy, and more often submitted to emergent procedures and "major" or "major-plus" complexity procedures. P-POSSUM value was higher in COVID-19-positive patients than in the intra-pandemic COVID-19-negative and the pre-pandemic cohorts [median (IQR)]: 1.79% (0.78–5.55) vs. 1.09% (0.59–3.02) and 1.09% (0.58–2.94), $p < 0.001$.

A total of 5318 surgical procedures were performed in the three cohorts, detailed in Table 2. During the pandemic period, emergency surgical activity was reduced by 21.9%, compared to the same period in 2019. The most frequent urgent procedures were: appendectomy, cholecystectomy, perianal surgery, hernia or incisional hernia repair, and colectomy.

3.2. Study outcomes

Main outcomes of the study population are shown in Table 3. 1271 patients (25.5%) presented postoperative complications, of which 631 were severe (12.7%). 205 patients died in the first 30 postoperative days (4.1%). The unadjusted incidences of complications, pulmonary complications , severe complications, need for postoperative ICU, length of stay, and postoperative mortality were greater in the COVID-19-positive cohort. Postoperative mortality of COVID-19-positive patients was greater for procedures considered as "minor", "moderate", and "major"; regarding "major-plus" procedures, postoperative mortality was similar between intra-pandemic COVID-19-positive and COVID-19-negative patients, but higher than pre-pandemic ones.

Procedures considered as emergent were associated with higher mortality than urgent ones in each of the three cohorts.

3.3. P-POSSUM mortality prediction

P-POSSUM score values were higher in the patients who died, compared to the survivors: 36% vs. 5% in the COVID-19-positive cohort; 23% vs. 3% in the pandemic COVID-19-negative cohort; and 26% vs. 4%

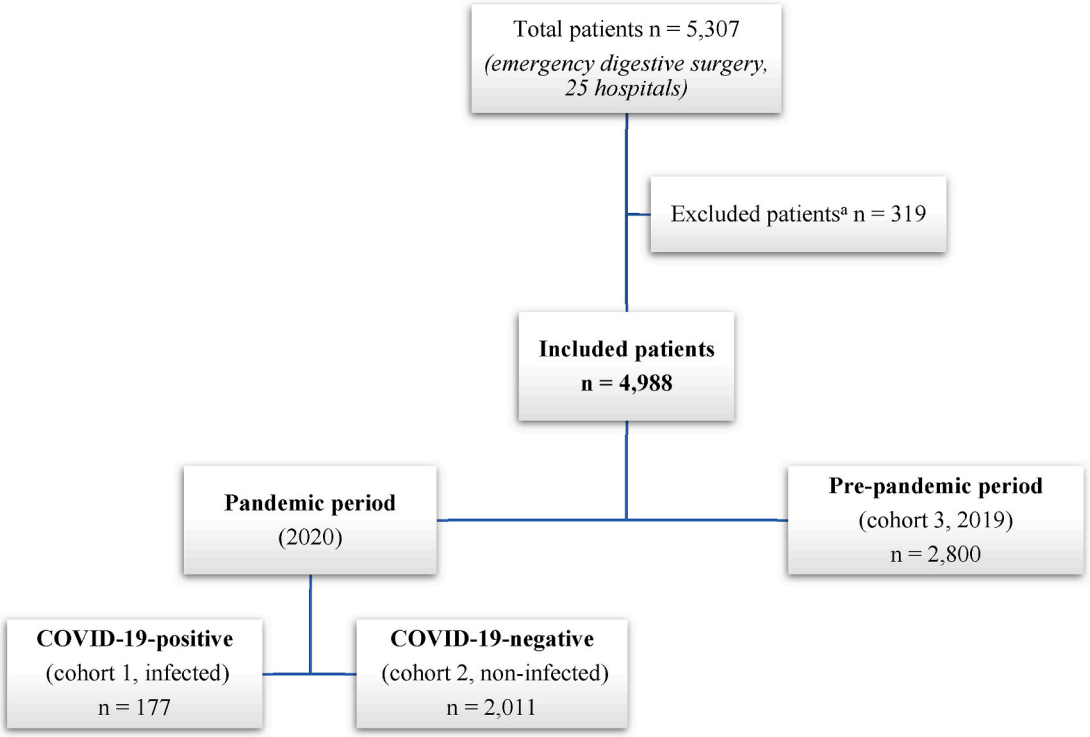


Fig. 1. Study flowchart.
[a] Patients without recording all the parameters necessary for the calculation of the P-POSSUM score or with less than 30 days of postoperative follow-up.

in the 2019 cohort.

The discriminative capacity of the P-POSSUM score, defined by the AUC value of the ROC curve, is shown in Fig. 2.

The calibration analysis did not show significant differences between the observed and estimated mortality rates in the COVID-19-positive cohort nor in the COVID-19-negative cohort, reflecting an adequate calibration (Fig. 3). The calibration of the P-POSSUM score in the 2019 cohort showed differences in the deciles with the highest predicted risk. According to the optimal cut-off point, the detailed predictive characteristics of the P-POSSUM score in each cohort (sensitivity, specificity, positive and negative predictive values, positive and negative likelihood ratios) are reflected in Table 4.

4. Discussion

The results of this cohorts' study support the use of P-POSSUM prognostic scoring system as a tool for estimating postoperative mortality in patients infected by SARS-CoV-2 submitted to emergency general and digestive surgery. It also proved its predictive value for COVID-19-negative patients in the stressful context of COVID-19 pandemic. The study is based on one of the most extensive series of consecutive patients operated on for emergency surgery during the COVID-19 pandemic period published to date and, to our knowledge, the first one analyzing the predictive capacity of the P-POSSUM score in this particular epidemiological context.

Emergency surgery is at higher risk of postoperative complications and mortality than elective procedures, due to the clinical deterioration secondary to the acute disease and the lack of a preoperative period to optimize comorbidities and correct organ dysfunction [3,30]. Postoperative mortality is the most significant prognostic measure in the field of surgical care. However, raw mortality rate is difficult to evaluate without adequate risk stratification. Different predictive scores for surgical risk have been designed to assign an adjusted risk of postoperative complications and/or mortality in surgical patients [1–6]. These scores can help to identify "high risk" patients who could benefit from intensified peri- and postoperative care, including early postoperative admission in ICU units or even referral to other centers [3]. Among them, the POSSUM and P-POSSUM scores, designed in the 1990s, constitute the most widespread and validated ones for patients undergoing emergency surgery [2,5,8,31]. Both scores are based on routine preoperative clinical and analytical data, supplemented with information obtained during the surgical intervention. They are easy to calculate, and multiple online and app options are available. However, their predictive capacity to estimate postoperative mortality in COVID-19-infected patients has not been evaluated.

Concomitant COVID-19 infection can worsen postoperative outcomes of surgical patients, as shown in a recent meta-analysis reporting a 24–28% mortality rate (odds ratio 7.9) [15]. In the present study, 30-day mortality of COVID-19-infected patients was 12.9%, greater than the 4.6% of contemporary COVID-19-negative ones. Based on similar findings, many authors and guidelines recommend delaying or avoiding surgery whenever possible in case of COVID-19 infection [12–14,16]. However, raw postoperative outcomes should be evaluated with caution, as COVID-19-positive patients in the present and previous studies were older, with more comorbidities, and higher anesthetic risk. It is unclear if increased postoperative mortality risk of COVID-19-infected patients is more in relation to their basal comorbidities and the severity of disease at presentation or to a specific effect of COVID-19 infection. Therefore, a general therapeutical recommendation is not acceptable for all potentially surgical COVID-19-positive

Table 1
Demographics, comorbidities, clinical, analytical and surgical variables, and P-POSSUM scores in the study population.

Variable	COVID-19-positive n = 177	COVID-19-negative n = 2011	2019 cohort n = 2800	p value[h]
Age, median (IQR), years	64 (49–73)	56 (40–72)	57 (40–73)	0.011[i]
Men, No. (%)	110 (62.1)	1193 (59.3)	1630 (58.2)	0.486
Women, No. (%)	67 (37.9)	818 (40.7)	1170 (41.8)	0.486
BMI[a], mean (SD), kg/m^2	27.9 (5.6)	27.2 (5.6)	27.3 (5.9)	0.306
BMI[a] ≥30 kg/m^2, No. (%)	36 (26.5)	335 (27.1)	424 (25.2)	0.097
ASA score[b], No. (%)				NA[j]
I	32 (18.2)	572 (28.6)	817 (29.4)	
II	62 (35.2)	818 (40.9)	1073 (38.6)	
III	59 (33.5)	507 (25.4)	735 (26.4)	
IV	22 (12.5)	98 (4.9)	147 (5.3)	
V	1 (0.6)	3 (0.2)	8 (0.3)	
Functional status[c], No. (%)				NA[j]
Independent	149 (84.2)	1822 (90.6)	2544 (90.9)	
Partially dependent	26 (14.7)	175 (8.7)	228 (8.2)	
Fully dependent	2 (1.1)	14 (0.7)	28 (1.0)	
Comorbidities, No. (%)				
Arterial hypertension[d]	78 (44.1)	672 (33.4)	971 (34.7)	0.016
Diabetes[d]	39 (22.0)	253 (12.6)	395 (14.1)	0.002
Active smoker	26 (14.7)	343 (17.2)	484 (17.3)	0.672
COPD	18 (10.2)	167 (8.3)	185 (6.6)	0.031
Cardiovascular disease[e]	31 (17.5)	233 (11.6)	377 (13.5)	0.027
Cardiac system, No. (%)				NAj
Normal (no failure)	131 (74.0%)	1580 (78.6%)	2099 (75.0)	
Diuretics, digoxin, antianginal or antihypertensive drugs	38 (21.5)	374 (18.6)	599 (21.4)	
Peripheral edema, anticoagulant, incipient cardiomegaly	5 (2.8)	53 (2.6)	91 (3.3)	
Elevated jugular venous pressure, cardiomegaly	3 (1.7)	4 (0.2)	11 (0.4)	
Respiratory system[f], No. (%)				NA[j]
Normal (no dyspnea)	153 (86.4)	1802 (89.6)	2560 (91.4)	
Dyspnea with exercise	13 (7.3)	152 (7.6)	171 (6.1)	
Limiting dyspnea	7 (3.9)	53 (2.6)	59 (2.1)	
Dyspnea at rest	4 (2.3)	4 (0.2)	10 (0.4)	
Systolic blood pressure, mean (SD), mmHg	126 (25.2)	127 (23.0)	126 (23.3)	0.319
Heart rate, mean (SD), beats/minute	87.8 (17.9)	85.7 (18.9)	84.0 (18.2)	0.001
GCS score, mean (SD)	13.9 (3.3)	14.9 (1.0)	14.9 (1.0)	<0.001
Preoperative analytical data, mean (SD)				
Sodium, mmol/L	138 (5.0)	139 (27.0)	143 (264)	0.702
Potassium, mmol/L	4.0 (0.6)	4.2 (3.2)	4.2 (5.8)	0.826
Urea, mmol/L	8.9 (8.5)	6.9 (5.4)	7.3 (13.8)	0.061
Leukocytes, x10^9/L	13.4 (6.8)	13.0 (6.0)	12.6 (5.5)	0.010
Hemoglobin, g/dL	11.7 (3.9)	11.5 (4.7)	11.6 (4.6)	0.757
CRP, mg/L	144 (272)	101 (138)	105 (185)	0.008
NLR	12.0 (10.5)	10.2 (12.6)	9.7 (10.2)	0.020
PLR	274 (208)	229 (215)	230 (253)	0.054
SII, x10^9/L	2964 (2954)	2635 (3768)	2514 (3411)	0.180
Lymphocytes, x10^9/L	1.5 (1.3)	1.9 (2.6)	2.2 (3.6)	0.001
Lymphopenia (<1.3 × 10^9/L), No. (%)	95 (54.6)	854 (42.9)	1171 (42.1)	0.006
Electrocardiogram, No. (%)				0.227
Normal	154 (87.0)	1825 (90.8)	2512 (89.7)	
Atrial fibrillation	13 (7.3)	99 (4.9)	135 (4.8)	
Any other change	10 (5.7)	87 (4.3)	153 (5.5)	
Surgical complexity[g], No. (%)				NA[j]
Minor	32 (18.1)	443 (22.0)	703 (25.1)	
Moderate	72 (40.7)	998 (49.6)	1318 (47.1)	
Major	67 (37.9)	518 (25.8)	697 (24.9)	
Major-plus	6 (3.4)	52 (2.6)	82 (2.9)	
Number of procedures, mean (SD)	1.1 (0.3)	1.1 (0.3)	1.1 (0.3)	0.231
Intraoperative blood loss, No. (%)				NA[j]
≤100 mL	129 (72.9)	1754 (87.2)	2372 (84.7)	
101–500 mL	37 (20.9)	211 (10.5)	325 (11.6)	
501–1000 mL	8 (4.5)	27 (1.3)	45 (1.6)	
>1000 mL	3 (1.7)	19 (0.9)	58 (2.1)	
Peritoneal soiling, No. (%)				0.003
None	65 (36.7)	910 (45.3)	1389 (49.6)	
Minor (eros)	45 (25.4)	465 (23.1)	585 (20.9)	
Localized purulent	38 (21.5)	417 (20.7)	532 (19.0)	
Diffuse purulent	29 (16.4)	219 (10.9)	294 (10.5)	
Malignancy, No. (%)				NA[j]
No	154 (87.0)	1863 (92.6)	2618 (93.5)	
Localized tumor	15 (8.7)	85 (4.2)	117 (4.2)	
Metastasis (nodal or disseminated neoplasia)	8 (4.5)	63 (3.1)	65 (2.3)	
Clinical priority, No. (%)				0.002
Urgent (during the first 24 h)	158 (89.3)	1916 (95.3)	2638 (94.2)	
Emergency (≤2 h)	19 (10.7)	95 (4.7)	162 (5.8)	
P-POSSUM, median (IQR), %	1.79 (0.78–5.55)	1.09 (0.59–3.02)	1.09 (0.58–2.94)	<0.001[i]

IQR: interquartile range; BMI: body mass index; SD: standard deviation; ASA: American Society of Anesthesiologists; COPD: Obstructive Chronic Pulmonary Disease; GCS: Glasgow coma scale; CRP: C-reactive protein; NLR: neutrophil-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio; SII: systemic immune-inflammation index (neutrophil x platelet/lymphocyte counts); P-POSSUM: preoperative predicted Portsmouth-POSSUM mortality; NA: not available.

[a] Data available in 77% of cases in the COVID-19-positive cohort, 61% of cases in the COVID-19-negative cohort, and 60% of cases in the 2019 cohort.

[b] Puntuación de la American Society of Anesthesiologists (ASA) [23].

[c] Functional status or functional dependency [24].

[d] Patient needing specific pharmacological treatment.

[e] Antecedent of ischemic heart disease, cerebrovascular accident (transient ischemic attack, stroke) or peripheral artery disease.

[f] Respiratory system: normal, no dyspnea and chest X-ray with no signs of COPD; dyspnea with exercise, dyspnea with exercise and/or chest X-ray with minimal signs of COPD; limiting dyspnea, limiting dyspnea (1 landing) and/or chest X-ray with moderate signs of COPD; dyspnea at rest, dyspnea at rest (>30 breaths/minute) and/or chest X-ray with fibrosis or consolidation.

[g] Complexity of surgical procedures was considered as minor, moderate, major or major-plus as defined originally in the POSSUM score [6]: minor: hernia or incisional hernia repair, perineal surgery; moderate: cholecystectomy, appendectomy; major: gastrointestinal perforation suture, intestinal resection, colectomy, main bile duct surgery, gastrectomy, lysis of adhesions, internal hernia repair, enterolithotomy, splenectomy or minor liver trauma, exploratory laparotomy/laparoscopy, surgical control of intra-abdominal bleeding; major-plus: pancreatectomy or pancreatic necrosectomy, damage control surgery (due to trauma, bleeding, ischemia or peritonitis).

[h] p value from Chi-squared test for categorical variables and from Student's t-test for continuous variables.

[i] p value from Mann-Whitney U test.

[j] p value not available due to insufficient sample size in some groups.

cases; it is of paramount importance to weigh the risk of performing surgery against the risk of avoiding or delaying it in each individual case.

To our knowledge, only one surgical prognostic score has been tested in COVID-19-positive patients, the COVIDSurg mortality score [32]. It is a machine-learning derived tool designed for different surgical

Table 2
Surgical procedures performed in the study population (5318 procedures performed in 4988 patients).

Surgical procedure and complexity[a]	COVID-19-positive n = 177	COVID-19-negative n = 2011	2019 cohort n = 2800
Minor complexity			
Perianal surgery	19	285	438
Hernia or incisional hernia repair	12	192	311
Moderate complexity			
Appendectomy	44	689	809
Cholecystectomy	31	317	502
Major complexity			
Colectomy	25	140	180
Intestinal resection	10	123	181
Lysis of adhesions or internal hernia repair	12	105	133
Gastrointestinal perforation suture	8	67	132
Other surgical procedures[b]	16	80	106
Surgical control of intra-abdominal bleeding	5	19	41
Exploratory laparotomy[c]	3	35	27
Splenectomy or minor liver trauma	1	11	24
Gastrectomy	1	16	14
Main bile duct surgery	1	4	10
Major-plus complexity			
Damage control surgery	5	44	67
Pancreatectomy or pancreatic necrosectomy	1	7	15

[a] Complexity of surgical procedures was considered as minor, moderate, major or major-plus, as defined originally in the POSSUM score [6]. The same patient may have required several surgical procedures during an intervention.

[b] The "other surgical procedures" category includes: debridement of skin and soft tissue infection or necrotizing fasciitis; colostomy or intestinal bypass; abdominal washout and drainage (abdominal sepsis); postoperative evisceration repair; hemostasis of surgical incision or abdominal wall bleeding; surgical airway; choleperitoneum; treatment of anastomotic leak; other surgical procedures considered as "major procedures".

[c] The "exploratory laparotomy" category includes: suspected intestinal perforation, anastomotic dehiscence or peritonitis (22 cases); peritoneal carcinomatosis (14 cases); massive intestinal ischemia (12 cases); suspected intestinal obstruction (9 cases); suspected intestinal ischemia (6 cases); other surgical procedures (2 cases).

specialties, emergency and elective procedures and without external validation, making its validity and applicability questionable. In the present study, the predictive capacity of the P-POSSUM score in estimating postoperative mortality for COVID-19-infected patients was good in terms of discrimination (AUC = 0.88), calibration (β = 0.97), sensibility (83%), and specificity (81%), similar to the capacity displayed by the same score applied to COVID-19-negative patients in this and previous studies [1,2,5,31]. Moreover, the predictive performance of P-POSSUM score was equal or greater than that demonstrated before the COVID-19 pandemic by other less spread surgical prognostic scores: the National Emergency Laparotomy Audit (NELA) score: AUC 0.83–0.86, sensibility 83.3%, and specificity 69.7% [1,31]; the American College of Surgeons-National Surgical Quality Improvement Program-Surgical Risk Calculator (ACS-NSQIP-SRC): AUC 0.80, sensibility 76.7%, and specificity 68.4% [1]; the Acute Physiology And Chronic Health Evaluation-II (APACHE-II) score: AUC 0.76, sensibility 65%, and specificity 72.2% [1]; the Surgical Risk Score (AUC 0.85) [2]; the Biochemistry and Haematology Outcome Model (BHOM) score: AUC 0.58–0.84 [2,31]; the Surgical Mortality Probability Model: AUC 0.77 [33]; and the Emergency Surgery Score: AUC 0.87 [34]. Finally, the predictive power showed by the P-POSSUM score in the present study was also similar or even higher than the capacity shown by mortality scales specifically designed for non-surgical COVID-19-infected patients, such as: 4C mortality score (AUC 0.77) [31]; CURB-65 score (AUC 0.82) [35]; Pneumonia Severity Index (AUC 0.82) [35]; MuLBSTA score (AUC 0.72) [35]; COVID-GRAM critical illness risk score (AUC 0.86) [35].

This study has some limitations. It only involves one country, a fact that could limit generalizability of the results. However, it represents a largely homogeneous population base and it could minimize selection bias. Its retrospective design is a further limitation, which was intended

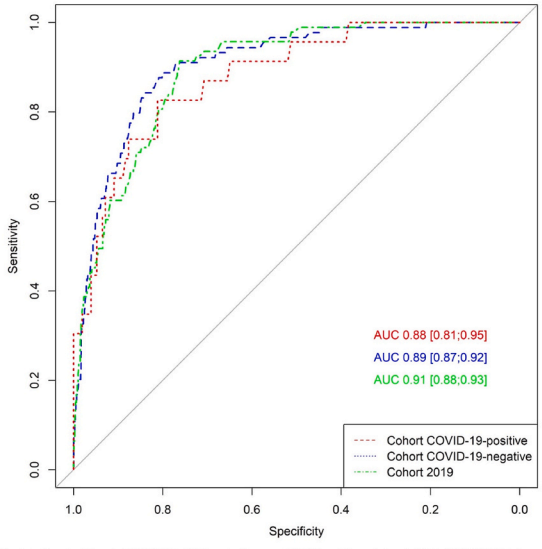
Table 3
Main outcomes of the study population.

Variable	COVID-19-positive n = 177	COVID-19-negative n = 2011	2019 cohort n = 2800	p value
Patientes with 30-day postoperative complications, No. (%, 95% CI)	75 (42.4, 35.1–50.0)	487 (24.2, 22.4–26.2)	709 (25.3, 23.7–26.9)	<0.001
Patients with pulmonary complications[a], No. (%, 95% CI)	32 (18.1, 12.9–24.7)	113 (5.6, 4.7–6.7)	156 (5.6, 4.8–6.5)	<0.001
Patients with severe complications[b], No. (%, 95% CI)	44 (24.9, 18.8–32.0)	243 (12.1, 10.7–13.6)	344 (12.3, 11.1–13.6)	<0.001
Need of postoperative ICU for ≥24 h, No. (%)	55 (31.4)	233 (11.6)	372 (13.3)	<0.001
Length of stay, median (IQR), days	7 (4–18)	4 (2–8)	4 (2–9)	<0.001
30-day rehospitalization, No. (%)	15 (9.9)	128 (6.7)	175 (6.5)	0.260
30-day surgical reintervention, No. (%)	10 (6.6)	105 (5.5)	145 (5.4)	0.818
30-day mortality, No. (%, 95% CI)	23 (12.9, 8.6–19.1)	93 (4.6, 3.8–5.7)	89 (3.2, 2.6–3.9)	<0.001

95% CI: confidence interval of 95%; ICU: intensive care unit; IQR: interquartile range.

[a] Pulmonary complications: respiratory infection or pneumonia, defined as purulent expectoration with positive bacteriological/virological culture, with or without changes in chest X-ray, or fever associated to pulmonary consolidation in chest X-ray; respiratory failure, defined as dyspnea requiring ventilator urgent support and/or PaO_2<60 mmHg and $PaCO_2$>45 mmHg without oxygen assistance; and pleural effusion/pulmonary atelectasis.

[b] Postoperative complications with Clavien-Dindo grade ≥ IIIA [26].



ROC: Receiver Operating Characteristic [26,27]; AUC: area under curve; 95% CI: confidence interval of 95%; P-POSSUM: Portsmouth-POSSUM score.

Fig. 2. ROC curves and AUC (with 95% CI) of P-POSSUM score in the three cohorts.

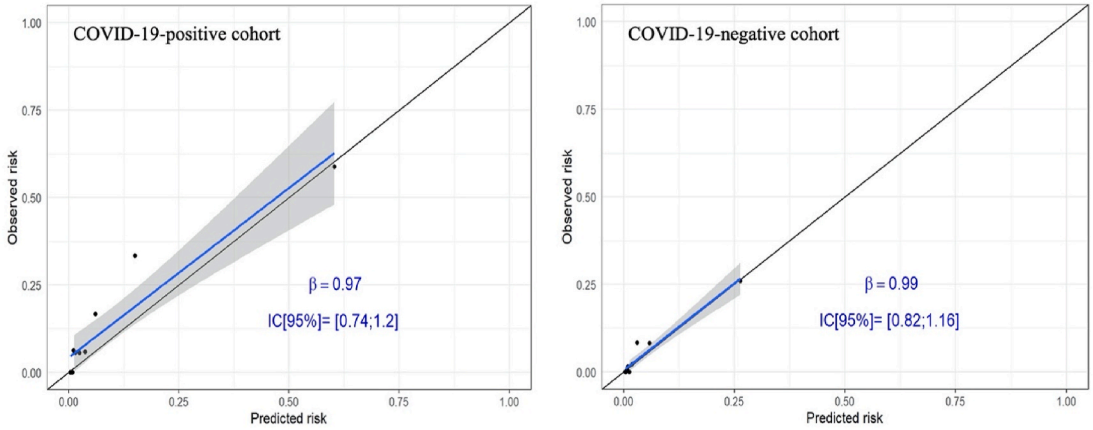


Fig. 3. Calibration plots of P-POSSUM score in COVID-19-positive and COVID-19-negative cohorts.

Table 4
Predictive characteristics of P-POSSUM score (30-day mortality) in the three cohorts.

Predictive characteristics	COVID-19-positive $n = 177$	COVID-19-negative $n = 2011$	2019 cohort $n = 2800$
AUC, value (95% CI)	0.88 (0.81–0.95)	0.89 (0.87–0.92)	0.91 (0.88–0.93)
Calibration, linear regression slope, β value (95% CI)	0.97 (0.74–1.2)	0.99 (0.82–1.16)	0.78 (0.74–0.82)
P-POSSUM cut-off point[a], %	5.2	2.7	3.4
Sensitivity, % (95% CI)	83 (61–95)	91 (84–96)	89 (80–94)
Specificity, % (95% CI)	81 (74–87)	76 (74–78)	80 (79–82)
Positive predictive value, % (95% CI)	40 (26–55)	16 (13–19)	13 (10–16)
Negative predictive value, % (95% CI)	97 (92–99)	99 (99–100)	100 (99–100)
Positive likelihood ratio, value (95% CI)	4.39 (3.01–6.40)	3.84 (3.47–4.26)	4.46 (4.02–4.96)
Negative likelihood ratio, value (95% CI)	0.21 (0.09–0.52)	0.11 (0.06–0.22)	0.14 (0.08–0.25)

AUC: area under ROC curve; 95% CI: confidence interval of 95%; P-POSSUM: Portsmouth-POSSUM score.

[a] Cut-off point of P-POSSUM score calculated by maximizing the Youden index (maximizing sensitivity and specificity) [29].

to be minimized by the thorough data quality control and the exclusion of patients with relevant missing variables. Besides, it must be noted that some relevant prognostic parameters not included in the P-POSSUM score were not recorded in the COVID-CIR register, such as nutritional state or clinical frailty. The applicability of the findings may be limited in the current context due to generalization of the COVID-19 vaccination and the natural immunity conferred by previous COVID-19 infection. However, as we found P-POSSUM score is a useful mortality predictor both in COVID-19-positive and -negative patients, it is presumable that it will also work for patients that suffered from COVID-19 in the past. Finally, the study did not provide a comparative cohort of potentially surgical patients submitted to conservative treatment.

5. Conclusions

The findings of the present cohort study suggest that the P-POSSUM score, a well-known and easily applicable risk-prediction tool, has a good capacity in estimating postoperative mortality in COVID-19-infected patients submitted to emergency general and digestive surgery. COVID-19-positive surgical patients with a high P-POSSUM score should be considered as high-risk patients and require closer postoperative monitoring for early detection of complications to reduce postoperative mortality.

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Ethical approval

The study protocol was approved by the Clinical Research Ethics Committee of the leading and collaborating centers (Ethics and Clinical Investigation Committee of the Hospital Universitari de Bellvitge, code PR169/20, date approval 05/05/20).

Research registration Unique Identifying number (UIN)

1. Name of the registry:
ClinicalTrials.gov Protocol Registration and Results System.
2. Unique Identifying number or registration ID:
NCT04479150.
3. Hyperlink to your specific registration (must be publicly accessible and will be checked):
https://clinicaltrials.gov/ct2/show/NCT04479150.

Guarantor

Zoilo Madrazo

Data statement

The datasets generated and analysed during the current study are not publicly available but are available from the corresponding author on reasonable request.

CRediT authorship contribution statement

Zoilo Madrazo: Conceptualization, Data curation, Investigation, Methodology, Validation, Visualization, Writing – original draft, preparation, Writing – review & editing. **Javier Osorio:** Conceptualization, Data curation, Funding acquisition, Investigation, Methodology, Validation, Writing – original draft, preparation, Writing – review & editing. **Sebastián Videla:** Conceptualization, Methodology, Validation, Resources, Writing – original draft, preparation, Writing – review & editing. **Beatriz Sainz:** Investigation. **Araceli Rodríguez-González:** Investigation. **Andrea Campos:** Investigation. **Maite Santamaría:**

Investigation. **Amalia Pelegrina:** Investigation. **Carmen González-Serrano:** Investigation. **Aurora Aldeano:** Investigation. **Aingeru Sarriugarte:** Investigation. **Carlos Javier Gómez-Díaz:** Investigation. **David Ruiz-Luna:** Investigation. **Amador García-Ruiz-de-Gordejuela:** Investigation. **Concepción Gómez-Gavara:** Investigation. **Marta Gil-Barrionuevo:** Investigation. **Marina Vila:** Investigation. **Arantxa Clavell:** Investigation. **Beatriz Campillo:** Investigation. **Laura Millán:** Investigation. **Carles Olona**: Investigation. **Sergi Sánchez-Cordero:** Investigation. **Rodrigo Medrano:** Investigation. **Camilo Andrés López-Arévalo:** Investigation. **Noelia Pérez-Romero:** Investigation. **Eva Artigau:** Investigation. **Miguel Calle:** Investigation. **Víctor Echenagusia:** Investigation. **Aurema Otero:** Investigation. **Cristian Tebé:** Data curation, Formal analysis, Methodology, Software, Writing – original draft, preparation. **Natàlia Pallarès:** Data curation, Formal analysis, Methodology, Software, Writing – original draft, preparation. **Sebastiano Biondo:** Conceptualization, Supervision.

Declaration of competing interest

The authors have no competing interests to declare.

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Appendix A. Supplementary data

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